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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/515,984 | 07/06/2005 | Carl-Fr Coester | FZ002-US | 6317 |

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| EXAMINER | |
|---|---|
| JEAN-LOUIS, SAMIRA JM | |
| **ART UNIT** | **PAPER NUMBER** |
| 4173 | |
| **MAIL DATE** | **DELIVERY MODE** |
| 11/26/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/515,984 | COESTER, CARL-FR | |
| | Examiner | Art Unit | |
| | Samira Jean-Louis | 4173 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11/08/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *32-42* is/are pending in the application.

4a) Of the above claim(s) *40-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Sheets(2)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election without traverse of group II (method for the treatment of Parkinson's Disease using nefazodone) in the reply filed on 11/08/07 is acknowledged. Claims 40-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group IV, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/08/07.

Claims 32-42 are currently pending in the application. However, due to a restriction requirement, claims 40-42 are withdrawn from further consideration and claims 32-39 are being examined on the merits herein.

Thus the requirement is deemed proper and is therefore made final.

### *Priority*

Acknowledgment is made of applicant's claim for foreign priority. It is noted, however, that applicant has not provided English translations of the German application 102232547 as required by 35 U.S.C. 119(b). Thus, the priority date of the instant invention is May 21, 2003 (the date of the PCT application). Without the English translation, one cannot ascertain if the instant invention is present in the German application. Therefore, art prior to the PCT date, but not before the date of the German application may be cited against the claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**Claims 32-38 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Nelson (U.S. 2004/0229908 A1) and Drugs@FDA Glossary of Terms in view of Dennis et al. (U.S. 6,143,325).**

Nelson teaches a method of treating Parkinson's disease comprising an active ingredient or ingredients combined with adjuvants, acceptable pharmaceutical salts thereof, and mixtures of the foregoing (see abstract, page 4, paragraph 0034 and page 5, paragraph 0078, lines 5-7 and claim 34). Nelson also teaches that preferred compounds such as dopamine and dopamine agonists (i.e. L-Dopa, see page 4, paragraph 0030, page 6, paragraphs 0083 and 0091 and page 9, paragraph 0166 vs. instant claim 33) and peripheral metabolism inhibitors such as 2-[3-[4[-(3-chlorophenyl)-1-piperazinyl]propyl]-5-ethyl-4(2-phenoxyethyl)-2H-1,2,4,-triazol-3(4H)-one (i.e. nefazodone; see page 7, paragraphs 0110 and 0129) of a daily dosage of about 50 mg to about 150 mg (instant claim 34) can be used in such composition. Nelson further teaches that this method of treatment further provides for a pharmaceutical composition administered orally in the form of a tablet (see page 12, paragraph 0200, lines 1-5).

Given that Nelson is silent to the definition of what an active ingredient entails, it is concluded that nefazodone is considered to be an active ingredient in the aforementioned composition since it is well known in the art than an active ingredient is a compound that provides pharmacological activity or other direct effect in the treatment of a disease as evidenced by the FDA glossary term (see http://www.fda.gov/cder/drugsatfda/glossary.htm). As a result, Nelson is considered to teach a nefazodone-containing composition of about 0.5 mg to about 1000 mg (instant claim 35) or preferably from about 2 mg to about 500 mg that may be administered in a single daily dosage (instant claim 37) or optionally given in divided doses two to four times a day (see page 12, paragraph 0201 vs. instant claim 36).

Nelson, however, does not specifically teach a method of treating Parkinson disease with the exact specific ranges of about 100 mg to about 800 mg or about 300 mg to about 600 mg of nefazodone.

Dennis et al., however, teaches the use of nefazodone hydrochloride as immediate release tablets to be dosed twice daily (see column 1, lines 28-30 vs. instant claim 36). Dennis et al. further teaches that nefazodone can be given up to 450 mg up to three times a day or that its daily dosage can fall within the range of 200 mg to 600 mg for the twice daily immediate release system or potentially as a single unit dosage form (see column 1, lines 64-66 and column 3, lines 40-47 vs. instant claims 34-37).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to practice the method of Nelson in view of the dosage optimization routine provided by Dennis et al. in order to achieve an enhanced therapeutic effect. Given that Nelson teaches a method of treating Parkinson disease using a nefazodone-containing compound, and Dennis et al. teaches various efficacious dosages and concentrations of nefazodone, one of ordinary skill would have been motivated to utilize the method of Nelson with the dosage of Dennis et al. with the expectation of providing a treatment that is therapeutically effective.

While the exact ranges of the ingredients are not disclosed by Nelson, he does suggest that dosage regimen may be adjusted to provide the optimal therapeutic response (see page 12, paragraph 0021, lines 13-17). Additionally, it is generally noted that differences in concentration do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of specific ranges of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.

**Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson (U.S. 2004/0229908 A1) as applicable to claims 32-38 above in view of Walraven (British Med. J., 2001, pg. 1-6).**

The Nelson reference is as discussed above and incorporated by reference herein. However, Nelson does not address a method further comprising administering a composition comprising a pharmaceutical agent selected from the group of pharmaceutical agents consisting of caffeine, acetyl salicylic acid or combinations thereof.

Walraven et al., however, teaches a study undertaken in order to determine the association between inhibition of serotonin reuptake by antidepressants such as nefazodone and upper gastrointestinal bleeding (see abstract and Discussion section, 2nd paragraph). Walraven, also discloses that serotonin can potentiate platelet aggregation. Importantly, Walraven et al. discloses that the study included patients who took the antidepressants such as nefazodone and acetylsalicylic acid (see page 3, table 1and page 5, table A2 vs. instant claim 39).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Nelson with acetylsalicylic acid given that Walraven discloses that serotonin reuptake inhibitors such as nefazodone can lead to increased platelet aggregation and ultimately lead to blood clotting. Given that Nelson teaches a method of treating Parkinson's disease using *a* nefazodone-containing

composition, and Walraven discloses that antidepressants such as nefazodone can lead to blood clotting, one of ordinary skill would have been motivated to utilize the method of Nelson with the an inhibitor of platelet aggregation such as acetylsalicylic acid with the expectation of providing a successful method of treating Parkinson disease that does not lead to cardiovascular adverse effects.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-5 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SJL

11/17/2007

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER